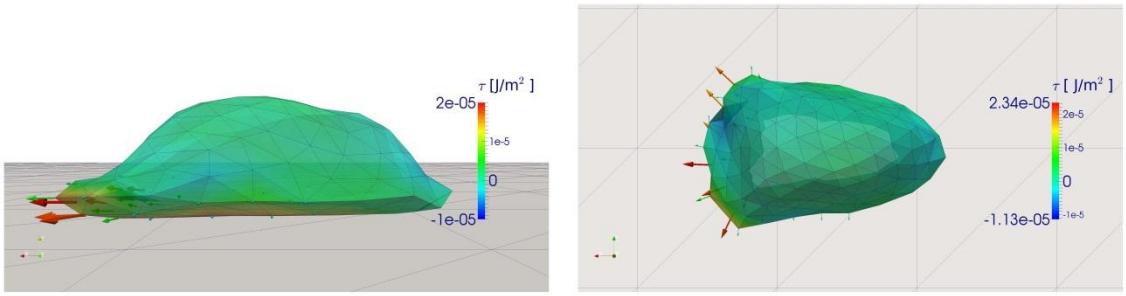
Cell migration investigated by a mechanistic 3D deformable cell model

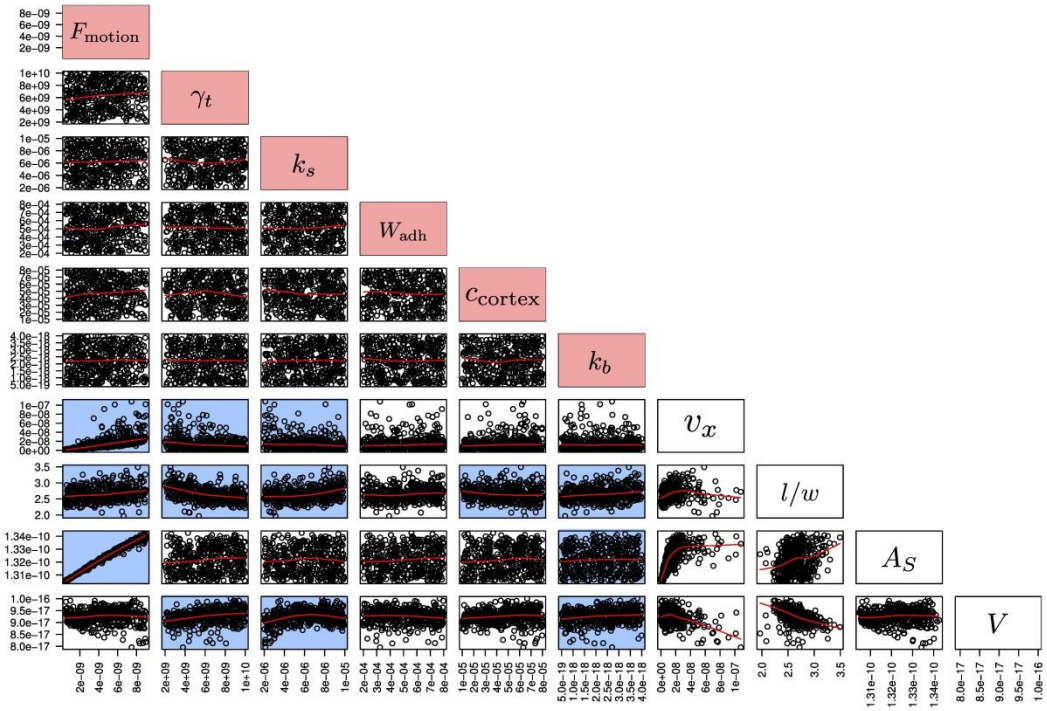
Tim Odenthal, Bart Smeets, Tommy Heck, Herman Ramon, Hans Van Oosterwyck
BMe, KU Leuven

The field of research concerned with cell migration and its determining factors tries to answer both fundamental as well as application driven questions, e.g. in the field of tissue engineering, wound healing and cancer treatment. More specifically, tip-cell migration in angiogenic sprouts poses interesting problems: How is the force generation of the cell regulated? How does the cell apply forces to the extracellular matrix (ECM) to propel itself forward? How does it degrade and to what extent does it rearrange the ECM locally? Due to the complexity of the system under study, it becomes necessary to formulate computational models that can help by condensing existing knowledge and providing a test-bed for hypotheses on the mechanisms for these phenomena.
Building further on the mechanistic model for passive cell spreading presented in[1,2], we explore a simple model for cell locomotion both on 2D substrates and in a 3D environment. A prescribed global propulsive force is distributed to those nodes from a triangulation of the cell's cortex, which are close to a cell-substrate contact. This results in a "polymerization pressure" which is biased with the given polarization of the cell.
A detailed study of the parameters governing adhesion, propulsion, and the cell's cortex elucidates the relative importance of cell (cortex) mechanical parameters for cell migration speed and the morphology of the migratory cell (see preliminary data on migration on a 2D substrate in the Figure). A first order analysis shows e.g. that all major mechanical properties of the cortex have a significant influence (shaded in blue) on the cell's average aspect-ratio (length/width).
Additional results of a study of a migrating cell within a 3D environment will be discussed.
References
[1] Odenthal, T. et al. “A DEFORMABLE CELL MODEL AND ITS APPLICATION TO INVESTIGATE INITIAL CELL SPREADING”. In: International Symposium on Computer Methods in Biomechanics and Biomedical Engineering. 2013.
[2] Odenthal, T., Smeets, B. et al. “Analysis of initial cell spreading using mechanistic contact formulations for a deformable cell model”. In: PLoS Computational Biology 9.10 (2013), e1003267.



(a) Side view

(b) Top view



(c) Parameter study

Figure 1: Preliminary results on cell migration model. Subfigures (a), (b) show one particular example of a migrating cell from this study in side and top view – the color scale representing the cortex tension. Subfigure (c) summarizes the results of a parameter study: The red-shaded parameters have been prescribed in a latin hyper-square experimental design and 436 simulations have been successfully run. The parameters represent the total motion force F_{motion}[N], tangential friction γ_t[N s/m^3], cortex stiffness k_s[N/m], adhesion surface energy W_{adh}[J /m^2], cortex viscous damping c_{cortex}[N s/m] as well as the apparent bending resistance k_b[J] of the cortex. The non-shaded parameters are time-averaged "readout variables", representing the cell velocity v_x[m/s], aspect-ratio l/w[–], cell surface area A_S[m^2] and cell volume V[m^3].